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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,762	03/19/2004	Yan Qi	A-72186/TAL/DCF	8100

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,762	QI ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,14-26 and 33-39* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-6,14,33-36* is/are rejected.

7)☒ Claim(s) *15-17 and 37-39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's responses and amendments of 9/25 and 9/29/06 are entered.

Claims 2-4, 7-13, and 27-32 are cancelled.

Claims 1, 5-6, and 15-17 are amended.

Claims 33-39 are newly presented.

Claims 1, 5-6, 14-26, and 33-39 are presently pending.

Election/Restrictions

Claims 18-26 remain withdrawn as being drawn to non-elected inventions.

Claims 1, 5-6, 14-17, and 33-39

are presently considered, however, Claims 15-17 and 37-39 are only considered to the point of being objected to, due to multiple dependency problems, as below.

This application contains claims 18-26 drawn to an invention nonelected with traverse in the response of 12/27/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

Claims 15-17 and 37-39 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claims. See MPEP § 608.01(n). Accordingly, claims 15-17 and 37-39 have not been further treated on the merits.

Claims 1, 5-6, 14, and 33-36 are presently considered on their merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-9 are rejected and newly added claims 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

(i) a method for inhibiting the development of adaptive CTL immunity to allogenic target cells exhibiting cell-surface expressed target cell specific antigens, comprising contacting the target cell with an expression vector comprising a cell-surface expressed CD8-alpha chain transgene, wherein said CD8-alpha chain is expressed on the surface of the cell, and thereby inhibits the subsequent development of adaptive CTL immunity to such cell-expressed antigens;

(ii) a method for specifically inhibiting the development of donor-induced adaptive CTL immunity to allogenic cells in a recipient, comprising transforming the cells of the donor allograft cells with a vector for expressing a CD8-alpha chain on the cell surface prior to transplantation, then transplanting the cells into the recipient, wherein said CD8-alpha chain is expressed on the surface of the cells and inhibits the development of adaptive CTL immunity to such cell-expressed antigens; and

(iii) a method for extending the survival of an allograft in a recipient, comprising similar steps to (ii), does not reasonably provide enablement for inhibiting any immune response (Claim 1 and dependent claims), any portion of the CD8-alpha chain, or any CTL response. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims.

With regard to the breadth of claim 1 and dependent claims, the rejections are maintained for reasons of record, as it is clear that only adaptive CTL immunity is affected, and not other forms of immune reaction.

With regard to any portion of the CD8-alpha chain, it is clear from the specification and art of record that the CD8-alpha chain extracellular domain is required to bind to the MHC of the T cell, and therefore the functional portion, which encompasses intracellular domains only, or transmembrane domains only, is not enabled for its full scope. Further a CD8-alpha extracellular domain must be attached to the cell membrane, otherwise the required interaction would not occur in a specific fashion, as taught by the specification.

With regard to any CTL response, applicant has demonstrated that antigen specific CTLs cannot be inhibited (e.g. paragraph 0173). Hence, not any response can be inhibited.

With regard to Claims 33-36, these claims are rejected for reasons of record, modified by the following explanation, required by way of amendment.

Claims 33-36 require intravascular injection of the vector encoding CD8-alpha at a site proximate to the target cells, at any time point (Claim 33) or prior to or during transplantation.

Claim 33 is not enabled for any point after 2 days post-transplant (e.g., Suryaprakash, et al. (1991) Science, 252: 1424-27, pp. 1424-25, paragraph bridging). Hence, it is clear that the Artisan would not reasonably predict any efficacious effect after 2 days after initiation.

Claims 33-36 encompass the in vivo transfection of these cells, however, as has been previously discussed it is not reasonably predictable that enough cells are transformed in any

particular case. To wit, Applicant's own examples demonstrate that particular tissues are refractory to transformation by any particular vector (EXAMPLE 3), and the various examples only demonstrate long-term incubation (multiple hours) in the presence of the vector. However, an IV injection, proximate to the site would necessarily encompass injection into the arterial/venous system at any point, because the blood would necessarily pass through the arteries and veins of the transplanted cells. However, for Applicant's specifically discussed adenoviral vectors, such would likely be cleared by the liver before reaching the tissue in most administrations. Further, in the best case scenario, that of injection in the artery(s) directly upstream of the organ, such a quick pass through the organ would not be reasonably predicted to transform enough cells, and would therefore have to pass through the rest of the body before reentering the organ, without transforming other tissues or being cleared by the liver/kidneys/macrophages of the body, in order to continue transformation to get enough cells transformed. Such is exacerbated by the fact that certain tissues directly transformed do have an immune response due to lack of enough cells being transformed (EXAMPLE 3). Applicant's explanation of a barrier (e.g., Declaration by Dr. Staerz of 9/29/06) fails to overcome this aspect, because the requisite number of cells still need to be transformed for any particular transplant. Further, these claims are subject to the same portion of CD8-alpha (extracellular domain attached to cell membrane) and the scope of any CTL response for reasons of record.

Response to Argument – Enablment

Applicant's argument of 9/25/06 and 9/29/06 have been fully considered but are not found persuasive.

Applicant argues that the claims have been amended to overcome the rejections (p. 6 of the 9/25/06 response).

Such is not persuasive. The examiner has shown that it has not been so fully amended and introduces new reasons for rejection.

Lastly, it is noted that the *ex vivo* claims are not rejected for the administration, as the Artisan would find it routine experimentation to find the amount of vector and time frame for transformation of the cells to receive an efficacious effect, whereas *in vivo* injections are undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, and 6 remain rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Application No. 2002/0127205 to Edge, et al, for reasons of record.

Further Claim 14 is newly rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Application No. 2002/0127205 to Edge.

To wit, with regard to Claim 14, Edge discloses human CD8-alpha, in paragraph 0059, where reference is made to Shiue, et al., for the CD8-alpha. Shiue teaches human CD8, including CD8-alpha chains. (The reference to Shiue, et al. (1988) J Exp Med, 168(6): 1993-2005 is attached for Applicant's convenience.)

Response to Argument – anticipation, Edge

Applicant's arguments of 9/25/06 and 9/29/06 have been fully considered but are not found persuasive.

Applicant argues that the claims only encompass expression of the CD8-alpha chain, and not heterodimers, which are argued to be what is taught by Edge (Applicant's argument of 9/25/06, p. 7, paragraphs 2-3).

Such is not persuasive. Applicant's claims are drawn to a vector encoding CD8-alpha, which would also encompass a vector encoding CD8-alpha and CD8-beta, and hence, the claimed invention is anticipated.

Applicant argues that Edge does not demonstrate CD8 expression, and therefore is largely speculative and not enabled.

Such is not persuasive. Edge teaches the invention. And the Artisan would find such to be enabled. To wit, it has been well known in the Art that CD8, or simply CD8-alpha ameliorates immune responses by CD8+ T lymphocytes (e.g., Suryaprakash, et al. (1991) Science, 252: 1424-27, p. 1424, col. 3, paragraphs 2-3). Hence, it is enabled.

Note: Claims 33-36 Free of Art of Record

It is noted that Edge (US Pat Applic No 2002/0127205) is not anticipated by Applicant's Claims 33-36. Such is because Edge only teaches IV administration of cells comprising the vector, and not the vectors themselves (e.g., paragraph 0108). Hence, such would require an obviousness-type rejection, however, such would also be inconsonant with the enablement

rejection provided above. Hence, Claims 33-36, while not enabled, are also free of the art of record.

Conclusions

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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